

WHAT IS CLAIMED IS:

1. A composition comprising:

(a) an admixture comprising a cancer, viral or parasitic antigen expressed by said cancer, virally or parasitic infected cells and a microfluidized antigen formulation, said antigen formulation comprising:

- (i) a stabilizing detergent,
- (ii) a micelle-forming agent, and
- (iii) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; and

(b) at least one agent which is capable of neutralizing or down regulating the activity of immunosuppressive factors.

2. The composition of claim 1 wherein said antigen formulation consists essentially of said stabilizing detergent, micelle-forming agent, and biocompatible oil.

3. The composition of claim 1 wherein the detergent is selected from the group consisting of TWEEN 80, TWEEN 20, TWEEN 40, TWEEN 60, Zwittergent 3-12, TEEPOL HB7 and SPAN 85.

4. The composition of claim 1 wherein said detergent is provided in an amount ranging from approximately 0.05 to 0.5%.

5. The composition of claim 4 wherein the amount of detergent is about 0.2%.

6. The composition of claim 1 wherein said micelle-forming agent has a hydrophile-lipophile balance of between 0 and 2.

7. The composition of claim 6 wherein the amount of said micelle-forming agent ranges from between 1.25 and 5%.

8. The composition of claim 1 wherein said micelle-forming agent is selected from the group consisting of poloxamer 401, PLURONIC L62Lf, PLURONIC L101, PLURONIC L64, PEG1000, TETRONIC 1501, TETRONIC 150R1, TETRONIC 701, TETRONIC 901, TETRONIC 1301 and TETRONIC 130R1.

9. The composition of claim 1 wherein the amount of said micelle-forming agent ranges from between 0.5 to 10%.

10. The composition of claim 1 wherein the oil exhibits an melting temperature of less than 65°C.

11. The composition of claim 1 wherein the oil is selected from the group consisting of squalane, eicosane, tetratetracontane, pristane, and vegetable oils.

12. The composition of claim 1 wherein the amount of oil ranges from between 1 and 10%.

13. The composition of claim 12 wherein the amount of oil ranges from between 2.5 and 5%.

14. The composition of claim 1 wherein the detergent is polysorbate 80 and the micelle-forming agent is poloxamer 401.

15. The composition of claim 14 wherein the oil is squalane.

16. The composition of claim 1 wherein the detergent is selected from the group consisting of TWEEN 20, TWEEN 40, and TWEEN 80, the oil is selected from the group consisting of squalane, eicosane, olive oil and pristane and the micelle-forming agent is selected from the group consisting of poloxamer 401, and PLURONIC L62LF.

17. The composition of claim 1 wherein said immunosuppressive factors is TGF $\beta$ .

18. The composition of claim 1 wherein said agent which is capable of neutralizing or down regulating the activity of tumor and host secreted immunosuppressive factors is an anti-TGF $\beta$  antibody, a TGF $\beta$ R-fusion protein, a TGF $\beta$  analog, a TGF $\beta$  binding protein or a TGF $\beta$ R blocking antibody.

19. The composition of claim 1 wherein said agent which is capable of neutralizing or down regulating or preventing activation of tumor and host secreted immunosuppressive factors is a thrombospondin peptide or a TGF $\beta$ R Fc-fusion protein.

20. The composition of claim 1 wherein said antigen formulation comprises squalane, TWEEN 80 and poloxamer 401.

21. The composition of claim 1 wherein said antigen is selected from the group consisting of gp100, MART-1/Melan A, gp75, tyrosinase, melanoma proteoglycan, MAGE, BAGE, GAGE, RAGE, N-acetylglucosaminyltransferase-V, mutated  $\beta$ -catenin, mutated MUM-1, mutated cyclin dependent kinases-4, p21 ras, BCR-abl, p53, p185 HER2/neu, mutated epidermal growth factor receptor, carcinoembryonic antigens, carcinoma associated mutated mucins, EBNA gene products, papillomavirus E7 protein, papillomavirus E6 protein, prostate specific antigens, prostate specific membrane antigen, PCTA-1, immunoglobulin idiotypes and T cell receptor idiotypes.

22. The composition of claim 1 wherein said composition is useful for treating cancer, viral or parasitic disorders.

23. In a method of treatment which includes the induction of a cytotoxic T-lymphocyte response wherein the improvement comprises (i) the administration of an adjuvant which induces a cytotoxic T-lymphocyte response and (ii) the administration of an antagonist of an immunosuppressive factor; wherein the administration of adjuvant and antagonist is effected sequentially or concurrently, and in any order.

24. The method of claim 23 wherein said secreted immunosuppressive factor is  $\text{TGF}\beta$ .

25. . The method of claim 24 wherein said adjuvant and antagonist are administered sequentially.

26. The method of claim 25 wherein the CTL inducing adjuvant is administered intradermally, intramuscularly or subcutaneously and the TGF antagonist is administered intravenously.

27. The method of claim 23 wherein said treatment comprises treating diseases selected from the group consisting of neoplasms or cancer, parasitic infection and viral infection.

28. The method of claim 23 wherein said treatment comprises restoring or boosting hematopoiesis.

29. The method of claim 27 wherein said cancer comprises breast cancer, brain cancer, cervical cancer, leukemia, lymphoma, prostate cancer, skin cancer, colon cancer, lung cancer, ovarian cancer, pancreatic cancer, liver cancer, bladder cancer, kidney cancer, myeloma, colorectal cancer or endometrial cancer.

30. The method of claim 27 wherein said viral infection comprises papillomavirus, Hepatitis, Herpes, cytomegalovirus, respiratory syncytial virus or HIV.

31. The method of claim 27 wherein said parasitic infection comprises malaria.

32. A method of treating neoplastic or cancerous growths comprising administering to a patient in need thereof:

(a) an admixture comprising a cancer or tumor antigen expressed by said cancer cells and a microfluidized antigen formulation, said antigen formulation comprising:

- (i) a stabilizing detergent,
- (ii) a micelle-forming agent, and
- (iii) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said admixture is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient which is specific for the cancer or tumor antigen contained in said admixture, and

(b) a therapeutically effective amount of at least one agent which is capable of neutralizing or down regulating the activity of tumor and host secreted immunosuppressive factors.

33. The method of claim 32 wherein said antigen is selected from the group consisting of gp100, MART-1/Melan A, gp75, tyrosinase, melanoma proteoglycan, MAGE, BAGE, GAGE, RAGE, N-acetylglucosaminyltransferase-V, mutated  $\beta$ -catenin, mutated MUM-1, mutated cyclin dependent kinases-4, p21 ras, BCR-abl, p53, p185 HER2/neu, mutated epidermal growth factor receptor, carcinoembryonic antigens, carcinoma associated mutated mucins, EBNA gene products, papillomavirus E7 protein, papillomavirus E6 protein, prostate specific antigens, prostate specific membrane antigen, PCTA-1, immunoglobulin idiotypes and T cell receptor idiotypes.

34. A method of treating neoplastic or cancerous growths comprising administering to a patient in need thereof the composition of claim 1 in an amount sufficient to induce a cytotoxic T-lymphocyte response.

5 35. A method of restoring or boosting hematopoiesis comprising administering to a patient in need thereof:

(a) an admixture comprising a cancer, viral or parasitic antigen expressed by said cancer, virally or parasitic infected cells and a microfluidized antigen formulation, said antigen formulation comprising:

- 10 (i) a stabilizing detergent,  
(ii) a micelle-forming agent, and  
(iii) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; wherein said admixture is administered to said patient in an amount sufficient to induce a cytotoxic T-lymphocyte response in said patient which is specific for the viral or cancer antigen contained in said admixture, and

15

(b) a therapeutically effective amount of at least one agent which is capable of neutralizing or down regulating the activity of tumor and host secreted immunosuppressive factors, wherein said admixture and said agent are administered separately or in combination, and in any order.

20

36. The method of claim 34, wherein said antigen is selected from the group consisting of gp100, MART-1/Melan A, gp75, tyrosinase, melanoma proteoglycan, MAGE, BAGE, GAGE, RAGE, N-acetylglucosaminyltransferase-V, mutated  $\beta$ -catenin,

mutated MUM-1, mutated cyclin dependent kinases-4, p21 ras, BCR-abl, p53, p185  
HER2/neu, mutated epidermal growth factor receptor, carcinoembryonic antigens,  
carcinoma associated mutated mucins, EBNA gene products, papillomavirus E7 protein,  
papillomavirus E6 protein, prostate specific antigens, prostate specific membrane antigen,  
5 PCTA-1, immunoglobulin idiotypes or T cell receptor idiotypes.

37. A composition comprising:

(a) an admixture comprising a cancer, viral or parasitic antigen expressed by  
said cancer, virally or parasitic infected cells and a microfluidized antigen formulation,  
10 said antigen formulation comprising:

- (i) a stabilizing detergent,
- (ii) a micelle-forming agent, and
- (iii) a biodegradable and biocompatible oil,

said antigen formulation being formulated as a stable oil-in-water emulsion; and

15 (b) one or more TGF $\beta$  antagonists.